REMARKS

Claims 1 and 3-8 are pending in the instant application. Claims 1 and 3-8 have been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Withdrawn Claim Rejections

Applicants acknowledge the withdrawal of the rejection of record under 35 U.S.C. 112, second paragraph. Applicants also acknowledge the withdrawal of the rejections of record under 35 U.S.C. 102(b) or 103(a) as being anticipated or obvious over Hannoush et al. or Wasner et al. Applicants further acknowledge the withdrawal of the rejection of record under 35 U.S.C. 103(a) as being unpatentable over Andreola et al. in view of Park et al. in further view of Hannoush et al.

II. Rejection of Claims Under 35 U.S.C. §103

Claims 1 and 3-8 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Hannoush et al. (Document AE, PTO-1449 filed 10/4/04) in view of Denisov et al. ((2001) *Nucl. Acids Res.* 29:4284-4293). The Examiner suggests that Hannoush et al. teach a duplex oligonucleotide comprising a ribonucleic acid, 4 nucleotides in length, wherein the duplex comprise 3', 5'-linked or 2', 5'-linked RNA wherein the duplex strands are linked by a tetranucleotide loop comprising SEQ ID NO:1. The Examiner acknowledges that Hannoush et al. do not teach a hairpin duplex comprising an arabinonucleic acid; however, Denisov et al. teach a hairpin duplex comprising an arabinonucleic acid and the duplex

can have increasing flexibility that elicits RNAse H activity. The Examiner suggests it would have been obvious to incorporate the arabinonucleic acid as taught by Denisov et al. into the hairpin duplex taught by Hannoush et al. with the motivation to increase flexibility and binding affinity to the target and further elicit RNase H activity.

Claims 1 and 3-8 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Wasner et al. (Document AM, PTO-1449 filed 10/4/04) in view of Hannoush et al. and further in view of Denisov et al. It is suggested that Wasner et al. teach a compound comprising two complementary strands 18-23 nucleotides in length, wherein the strands can be RNA or DNA or both and further wherein the strands are 3',5'-linked or 2',5'-linked nucleic acids. The Examiner acknowledges that Wasner et al. do not teach loop regions comprising SEQ ID NO:1 or self-complementary regions comprising arabinonucleic acid; however, Hannoush et al. teach the stabilizing effects of SEQ ID NO:1 and Denisov et al. teach a hairpin duplex comprising an arabinonucleic acid that is a substrate for RNAse H. It is suggested that it would have been obvious to incorporate the stabilizing tetranucleotide loops (SEQ ID NO:1) of Hannoush et al. and an arabinonucleic acid as taught by Denisov et al. into the duplex taught by Wasner et al. to produce a stable, flexible molecule with RNAse H activity.

Claims 1 and 3-8 have further been rejected under 35 U.S.C. 103(a) as being unpatentable over Wasner et al. in view of Hannoush et al. and in further view of Ray et al. ((2000) *FASEB J.* 14:1041-1060). It is suggested that Wasner et al. teach a compound comprising two complementary strands 18-23 nucleotides

in length, wherein the strands can be RNA or DNA or both and further wherein the strands are 3',5'-linked or 2',5'-linked. The Examiner acknowledges that Wasner et al. do not teach either strand of the antiparallel complementary oligonucleotide comprises a peptide nucleic acid; however, Hannoush et al. teach the stabilizing effects of SEQ ID NO:1 and Ray et al. teach incorporation of peptide nucleic acid into a duplex to increase the duplex stability and gene sequence specificity.

Applicants respectfully traverse these rejections.

To establish a prima facie case of obviousness, three basic criteria must be met. *First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.* Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicants' disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP 2142.

Hannoush et al. teach single hairpin loop structures composed of DNA, RNA, or both, wherein the loop region comprises SEQ ID NO:1, and the molecule *inhibits RNase H activity*. Similarly, Wasner et al. teach *RNase H inhibitors* composed of DNA:DNA, RNA:RNA, RNA:DNA, RNA:2',5'-RNA, and DNA:2',5'-RNA duplexes lacking hairpin structures. In contrast, Denisov et al. teach ANA:RNA and 2'F-ANA:RNA hybrids that elicit RNase H activity. See last sentence of the abstract. Likewise, Ray et al.

teach PNA/DNA chimeras for stimulating RNase H activity (see page 1049, second column under heading "RNase H").

The courts have held that there must be evidence that "a skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art reference for combination in the manner claimed." *In re Rouffet*, 149 F.3d at 1357, 47 USPQ2d at 1456. In this regard, Applicants were confronted with the problem of inhibiting RNase H activity. As such, the skilled artisan, confronted with the same problem as Applicants would *not* be motivated to combine the *inhibitory* structures of Hannoush et al. and Wasner et al. with the arabinonucleic acid of Denisov et al. or peptide nucleic acid of Ray et al. because Denisov et al. and Ray et al. teach the advantages of using arabinonucleic acid and peptide nucleic acid, respectively, in molecules for eliciting RNase H activity. Because the molecules of Hannoush et al. and Wasner et al. and the molecules of Denisov et al. and Ray et al. have opposing activity, there would no reasonable expectation of success that replacing the RNA or DNA of Hannoush et al. and Wasner et al. with the arabinonucleic acid of Denisov et al. or peptide nucleic acid of Ray et al. would provide a molecule capable of inhibiting RNase H activity.

Moreover, as acknowledged by the Examiner, Ray et al. disclose the use of peptide nucleic acids for antigene and antisense applications because peptide nucleic acids have very specific interactions with DNA and RNA. In this regard, replacing the RNA or DNA of Wasner et al. and Hannoush et al. with the peptide nucleic of Ray et al. would render the inhibitory ligands

of Hannoush et al. and Wasner et al. unsatisfactory for their intended use because the peptide nucleic acids of Ray et al. impart an antisense effect based upon their very specific interactions with DNA and RNA. In making a modification to a prior art reference to arrive at the claimed invention, MPEP 2143.01 states that if the "proposed modification would render the prior art invention being modified unsatisfactory for its intended use, then there is no suggestion or motivation to make the proposed modification." Accordingly, there is simply no suggestion or motivation in the cited prior art references to make the proposed modification.

As there is no suggestion or motivation to combine the teachings of Denisov et al. or Ray et al. with that of Wasner et al. and/or Hannoush et al. to produce, with a reasonable expectation of success, a composition for inhibiting the RNase H activity of a retroid virus reverse transcriptase these references fail to make obvious the instant invention in accord with MPEP 2142. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

II. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record.

Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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